

REMARKS

Favorable reconsideration of this application, in light of the preceding amendments and following remarks, is respectfully requested.

Claims 1, 2, 5-8, 11, 12, 17, 19-21, and 24-30 are pending in this application. Claims 1, 2, 5-8, 11, 12, 17, 19-21, and 24-28 have been withdrawn from consideration. Claim 29 is amended. No new matter is added. Claim 29 is the sole independent claim.

Example Embodiments of the Present Application

Example embodiments recite a method of modulating immunological activities consisting of transforming yeast cells with an amino acid sequence including SEQ ID NO.1, expressing a recombinant protein, and orally administering the recombinant protein isolated from the yeast cells or the yeast cell expressing the recombinant protein. Example non-limiting embodiments of this feature are discussed, for example, in paragraphs [0043] to [0049], and FIGS. 1 and 2 of the instant specification.

The SEQ. ID No. 1 has advantages such as efficiently using fungi to produce the fungal immunomodulatory protein (FIP). The conventional method of producing FIP is time-consuming and costly. Yeast is used to produce the FIP in example embodiments, because (a) the yeast and Ling-Zhi both belong to the fungi species and (b) yeast is safe for direct oral administration without an extraction and purification process. However, when integrating the wild type Ling-Zhi-8 nucleotide codon into yeast, the FIP producing rate is not satisfied and not suitable for massive production, because of the inclination of yeast for a specific codon. Thus, the wild type Ling-Zhi-8

nucleotide codon has been modified in SEQ ID NO. 1 to include the codon that was better expressed in fungi based on its high tRNA translation efficiency.

Further, as seen in example 3, section 73 of the present specification, the improved FIP nucleotide codon, SEQ ID NO: 1, can be highly expressed in yeast compared to the original wild type Ling-Zhi-8 nucleotide codon in yeast. After the modification of FIP codon, the FIP can be produced in yeast with better efficiency, and commercial production can be improved.

Rejections under 35 U.S.C. §103

Claims 29-30 are rejected under 35 U.S.C. §103(a) as being unpatentable over Evans et al (US Patent Number 5,928,896, hereinafter “Evans”) and Murasugi et al (Journal of Biological Chemistry Vol. 256, No. 4, pp 2486-2593, 1991, hereinafter “Murasugi”) in view of Egel-Mitani et al (Gene Vol. 73, pp 113-120, 1988, hereinafter “Egel-Mitani”).

In the Office Action, the Examiner admits that neither Evans nor Murasugi teach SEQ. ID NO.: 1, but relies on Egel-Mitani to teach this feature of claim 29. According to the Examiner, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have taken the DNA sequence for Ling-Zhi 8 as taught by Murasugi and optimize it for expression in a yeast cell as taught by Egel-Mitani to arrive at the claimed nucleotide sequence.

Evans teaches compositions of immunomodulatory peptides comprising Ling-Zhi-8 for oral administration. Murasugi discloses the nucleotide sequence encoding the amino acid sequence of Ling-Zhi-8 and its recombinant expression. Egel-Mitani teaches optimizing of codon usage when expressing heterologous genes in *Saccharomyces cerevisiae*. However, neither Evans, Murasugi nor Egel-Mitani teach

or suggest oral administration of Ling-Zhi-8 without any forms of protection. The combination of these citations thus does not disclose or suggest every recited limitation of the present invention.

Furthermore, Applicants respectfully submit that the Examiner does not provide a clear rationale including articulated reasoning that one of ordinary skill in the art would have been motivated to make the proposed combination of Evans, Murasugi and Egel-Mitani. Instead, the Examiner makes the conclusory statement that it would have been obvious to one skilled in the art to make the proposed combination of references in order to optimize expression of the DNA sequence in Murasugi in a yeast cell as taught by Egel-Mitani and to administer the resulting expressed protein orally in view of Evans.

However, without a clear rationale for making the proposed combination, the Examiner could render obvious every combination, and a requirement for some technical or logical motivation absent guidance provided by the present specification for making the combination would be effectively removed. See MPEP § 2143.01; citing *Ex parte Levingood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) ("[a] statement that modifications of the prior art to meet the claimed invention would have been 'well within the ordinary skill of the art' at the time the claimed invention was made' because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references") and *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006) ("[r]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.").

Therefore, Applicants respectfully submit that neither Evans, Murasugi, Egel-Mitani nor the combination thereof anticipate nor render obvious the limitations of amended claim 29.

Claim 30, dependent on independent claim 29, is patentable for the reasons stated above with respect to claim 29 as well as for their own merits.

The Applicants, therefore, respectfully request that the rejection to Claims 29-30 under 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

In view of the above remarks and amendments, the Applicants respectfully submit that each of the pending objections and rejections has been addressed and overcome, placing the present application in condition for allowance. A notice to that effect is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact the undersigned.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Erin G. Hoffman, Reg. No. 57,752, at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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By

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